Remarks

Reconsideration and withdrawal of the rejections set forth in the Office action dated March 28, 2006 are respectfully requested.

I. Amendments

Claim 29 is canceled.

Claims 21 and 27 are amended to recite the agent is a Pep5 polypeptide having the sequence of SEQ ID NO:2, or a sequence derived therefrom by one or several amino acid substitutions, deletions, and additions which retains the biological activity of Pep5. Basis for these amendments can be found in paragraph [0472].

Claims 25-26 are amended to more clearly define the claims.

Claim 28 is amended to depend from claim 22. Claim 28 is further amended for proper antecedent basis.

New claim 263 finds basis in original claim 180.

New claims 264-265 find basis in paragraphs [0718] and [0723].

No new matter is added by way of these amendments.

II. Objections to the Claims

Claim 28 was objected to under 37 C.F.R. § 1.75(c) as being in improper dependent form. The amendments to claim 28 obviate this objection.

III. Priority

Applicants are preparing a translation of the Japanese priority application, which will follow under separate cover. When the translation is received, Applicants will have complied with all of the requirements of 35 U.S.C. § 119(a)-(d) for foreign priority.

IV. Rejection under 35 U.S.C. §112, first paragraph

Claims 21-22 and 25-29 were rejected under 35 U.S.C. §112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 21-22 and 25-29 were further rejected under 35 U.S.C. §112, first paragraph, allegedly because the specification does not enable any person skilled in the art to which it pertains, or with which it is most connected to make and use the invention commensurate in scope with the claims.

These rejections are respectfully traversed.

A. Written Description

Claims 21 and 27, as amended, clarify the agent is a Pep5 polypeptide having the sequence of SEQ ID NO:2, or a sequence derived therefrom by one or several amino acid substitutions, deletions, and additions which retains the biological activity of Pep5. All of the members of the claimed genus share a common function (inhibiting a p75 signal transduction pathway) and structure (a Pep5 polypeptide of a specific sequence or derived therefrom).

With regard a sequence derived from Pep5, one skilled in the art would readily be able to determine the motifs of proteins that are important for activity and would recognize probable fragments that would retain activity. Furthermore, the biological activity of a Pep5 polypeptide for use in the claimed method can be easily confirmed. Therefore, one skilled in the art would be easily able to make and use the Pep5 polypeptide encompassed by the recitations of the claims.

Accordingly, one skilled in the art would understand that Applicants were in possession of the invention as presently claimed at the time of filing.

B. Enablement

The first paragraph of 35 U.S.C. §112 requires that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention without undue experimentation (e.g., *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir., 1991).

The enablement requirement is met if the description enables any mode of making and using the claimed invention (*Engel Industries, Inc. v. Lockformer Co.*, 946 F.2d 1528, 20 USPQ2d 1300 (Fed. Cir. 1991).

The Examiner acknowledges that the specification is enabling for the polypeptide SEQ ID NO:2 or anti-p75NTR antibodies, or Pep5 with an alanine residue added to the C-terminal end, or residues 273-427 of SEQ ID NO:4. However, the Examiner asserts that the application does not provide enablement for "all agents, unlimited by structure, which are capable of inhibiting p75 signal transduction pathways."

Claims 21 and 27 are amended to recite the agent is a Pep5 polypeptide having the sequence of SEQ ID NO:2, or a sequence derived therefrom by one or several amino acid substitutions, deletions, and additions which retains the biological activity of Pep5. Screening a sequence derived from a Pep5 polypeptide having the sequence of SEQ ID NO:2, which retains the biological activity of Pep5 is well within the skill of those in the art based on the guidance provided in the specification.

Of note, the DeFreitas reference was cited by the Examiner to demonstrate that "inhibiting the p75 pathway by addition of anti-p75 Fab fragments decreases survival." However, page 5123, second column clearly states that the antibodies are added to prevent the interaction of BDNF with p75. Thus, preventing BDNF binding results in lowering the survival of neurons, not the addition of antibodies which interact with p75 as asserted.

In light of the teaching in the specification and Applicant's amendments, Applicants submit that the present claims satisfy the requirements of §112, first paragraph and respectfully request that the rejections be withdrawn.

V. Rejection under 35 U.S.C. § 112, second paragraph

Claim 28 was rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

The Examiner first objected to the language "in the nerve" in claim 28 as lacking antecedent basis. Claim 28 as amended, provides proper antecedent basis for the objected language.

In view of the above, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

VI. Rejection under 35 C.F.R. § 102

Claim 27 was rejected under 35 U.S.C. §102(b) as allegedly anticipated by Ilag *et al.* (*Biochemical and Biophysical Research Communications*, 255:104-109, 1999).

Claims 21-22 and 25-28 were rejected under 35 U.S.C. §102(e) as allegedly anticipated by Bredesen (U.S. Patent Publication 2004/0192889).

These rejections are respectfully traversed.

A. The Present Application

The present claims relate to a composition for regenerating nerves, comprising an agent capable of inhibiting a p75 signal transduction pathway, wherein the agent is a Pep5 polypeptide having the sequence of SEQ ID NO:2, or a sequence derived therefrom by one or several amino acid substitutions, deletions, and additions which retains the biological activity of Pep5; and wherein the agent comprises a PTD domain (claim 21) and a composition for regenerating nerves comprising an agent capable of inhibiting a p75 signal transduction

pathway, wherein the agent is a Pep5 polypeptide having the sequence of SEQ ID NO:2, or a sequence derived therefrom by one or several amino acid substitutions, deletions, and additions which retains the biological activity of Pep5, wherein the agent comprises a PTD domain, and wherein the composition is suitable for in vivo or in vitro administration forms (claim 27).

B. The Prior Art

ILAG ET AL. describe selection of a peptide ligand to the p75 neurotrophin receptor death domain and determination of its binding sites by NMR.

BREDESEN discloses compositions and methods for modulating apoptosis.

C. Analysis

According to the M.P.E.P. § 2131, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference".

1. Rejection over Ilag *et al.*

Ilag *et al.* fail to teach an agent bound to a PTD domain.

2. Rejection over Bredesen

Bredesen fails to teach that the agent is a Pep5 polypeptide.

Accordingly, Applicants submit that standard of strict identity to maintain a rejection under 35 U.S.C. § 102 has not been met. Withdrawal of the rejections under 35 U.S.C. § 102 is respectfully requested.

VII. Rejection under 35 C.F.R. § 103

Claims 21-22 and 25-29 were rejected under 35 U.S.C. §103 as allegedly obvious over Ilag *et al.*, Schwarze *et al.* (*Science*, 285:1569-1572, 1999), Voet *et al.* (Biochemistry, Second Edition, 1995, pp. 58-59), and Bertin *et al.* (U.S. Patent Application No. 2002/0061833).

Claims 21-22 and 25-28 were rejected under 35 U.S.C. §103 as allegedly obvious over Bredesen.

These rejections are respectfully traversed.

A. The Present Application is described above.

B. The Cited References

ILAG ET AL. is described above.

BREDESEN is described above.

SCHWARZE ET AL. describe fusion proteins that contain an NH_2-terminal 11-amino acid protein transduction domain (PTD) for transduction of proteins.

VOET ET AL. list the amino acids and their residue mass.

BERTIN ET AL. relate to a method for determining whether a test compound alters the binding of CARD-3 to p75.

C. Analysis

According to the M.P.E.P. § 2143, "to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art references (or references when combined) must teach or suggest all the claim limitations."

1. Rejection over Ilag *et al.*, Schwarze *et al*, Voet *et al.*, and Bertin *et al.*

The combination of Ilag *et al.*, Schwarze *et al.*, Voet *et al.*, and Bertin *et al.* fails to show or suggest the claims as a whole, including the nature of the results obtained. Ilag et al. describes selection of a Pep5 sequence by SIP. The peptide was found to be specific towards the p75-ICD. However, Ilag et al. makes no

mention of the sequence comprising a PTD domain as presently claimed. Nor do the Schwarze *et al.*, Voet *et al.*, and Bertin *et al.* references provide the missing teaching. Specifically, although Schwarze *et al.* teach fusion proteins containing an 11-amino acid PTD, this reference merely describes the introduction of the proteins into cells. One skilled in the art would have no way of knowing, absent a "try and see" approach, that the proteins will retain their function. This is especially relevant to the agents of the present invention, which are involved in the signal transduction pathway acknowledged by the Examiner as complex. Nor do any of the other cited references make any mention of a PTD fusion protein.

Nor does the teaching in the combined references provide an expectation of a successful composition for regenerating nerves. Ilag *et al.* are limited to a discussion of the physiological role of Pep5 and make no mention of regenerating nerves. Schwarze *et al.* are not concerned with the biological function of the fusion proteins and make no mention of regenerating nerves. Voet *et al.* merely gives some physical data for the amino acids. Bertin *et al.* are concerned with proteins which bind to the intracellular domain of p75 to inhibit cell death. Thus, the only reference that makes any mention of a Pep5 agent, namely Ilag et al., provides no guidance for the claimed composition.

2. Rejection over Bredesen

As noted above, Bredesen fails to show or suggest a composition for regenerating nerves comprising an agent that is a Pep5 polypeptide.

In view of the above, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 103.

VIII. Conclusion

In view of the foregoing, Applicants submit that the claims pending in the application are in condition for Allowance. A Notice of Allowance is therefore respectfully requested.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4410.

Respectfully submitted,
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Date: June 28, 2006

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